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| EXAMINER | |
|---|---|
| HELMER, GEORGIA L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1638 | |

DATE MAILED: 05/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/053,266 | HEINZ ET AL. | |
| | Examiner | Art Unit | |
| | Georgia L. Helmer | 1638 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 January 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *17 January 2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of the Claims*

*1.* Claims 1-25 are pending and are examined in the instant action.

*2.* Claims 4-25 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend on another multiple dependent claim. See MPEP § 608.01(n). In the interest of compact prosecution, the claim will be treated on the merits. Such treatment does not relieve Applicant of the responsibility to respond to this objection.

### *Information Disclosure Statement*

3. Applicant's IDS filed 17 January 2002 is acknowledged and a signed copy included herewith.

### *Priority*

4. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has

become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

5. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in the European Patent Office on 20 July 1999. It is noted, however, that applicant has not filed a certified copy of the priority document, EP99114074.0 application as required by 35 U.S.C. 119(b).

### *Drawings*

6. The informal drawings are not of sufficient quality to permit examination. Accordingly, new drawings are required in reply to this Office action. Figures 1 and 2 are not of sufficient quality to permit examination.

Applicant is given a TWO MONTH time period to submit new drawings in compliance with 37 CFR 1.81. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a). Failure to timely submit new drawings will result in **ABANDONMENT** of the application.

### *Claim Rejections - 35 USC § 101*

7. Following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 23-25 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 23 is drawn to the harvestable parts or propagation material of a transgenic plant comprising at least one recombinant DNA molecule. Propagation material includes both transgenic and wild-type gametes, which will produce seed which may not be transgenic. The seed is the product of segregation of alleles, and because the seed has not been raised under selective conditions, some seed will not contain the transgene(s). Rather this seed will be identical to the wild-type parent, which is a product of nature. See American Wood v. Fiber Disintegrating Co., 90 U.S. 566 (1974), American Fruit Growers v. Brogdex Co., 283 U.S. 2 (1931), Funk Brothers Seed Co. v. Kalo Inoculant Co., 33 U.S. 127 (1948), Diamond v. Chakrabarty, 206 USPQ 193 (1980).

Claims 24 and 25 are drawn to a "use" which is not one of the five statutory classes of patentable subject matter.

8. Claims 24 and 25 also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a patentable asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

***Claim Rejections - 35 USC § 112-2***

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-25 are rejected under 35 USC § 112-2 for the following reasons

Claim 1 lacks agreement between the preamble and positive method steps. "Linum genus" plants are set forth in the preamble but appears nowhere else in the claim. Step (a), "introducing" recites "plant cells" generally. Furthermore, the method steps are not in proper order. The proper order of the steps as they would occur naturally in this process is

(a) Introducing ....,

(b) inducing ..,

(i) culturing the calli on a medium containing a first antibiotic,

(ii) transferring calli or shoots to medium containing a second antibiotic which is different from the first antibiotic, and

(c) thereby regenerating transgenic plants from the induced callus.

All claims dependent thereon are also rejected.

In claims 15-17, "NAA", TDZ, BAP are abbreviations or acronyms. The full name should be spelled out at least once, preferably at the first recitation of the abbreviation. This should be followed by the abbreviation in parentheses; suggested language is "napthalene acetic acid (NAA)".

Corrections or clarifications are required.

### *Claim Rejections - 35 USC § 112 Enablement*

11. Following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method of generating transgenic Linum usitatissimum (flax) plant cells comprising introducing Agrobacterium tumefaciens containing a binary vector bearing neomycin phosphotransferase gene comprising which confers resistance to kanamycin,160 mg/l, and G418, 60 mg/l, into hypocotyl segments, by coculturing for 4 days, transfer of cocultured material to medium containing a combination of the auxin NAA at 0.075 mg/l, the cytokinin benzylaminopurine at 1 mg/l, and kanamycin at a concentration of 160 mg/l for 6 weeks, followed by transferring selected calli or shoot material to medium containing a second antibiotic, G418, 60 mg/l, and rooting selected calli or shoots to produce a whole plant, as described in the specification (pages 20, Example 2, through page 28), does not reasonably provide enablement for the broad scope of the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Enablement is considered in view of the *Wands* factors (MPEP 2164.01(a)).

*The breadth of the claims*: The claims are drawn to a method for generating transgenic plants of the genus Linum comprising introducing a recombinant DNA binary vector comprising a selectable marker which confers resistance to at least one antibiotic into plant cells, induction a transgenic callus from the cells thereof and regenerating transgenic flax plants after culturing the calli on a medium containing at least a first antibiotic, and transferring the calli or shoots onto a medium containing a second antibiotic which is different from the

first antibiotic. The claims are drawn broadly to all Linum genus plants, including linseed, flax, and Linus usitatissimum, to all explants including leaves, roots, stems, hypocotyls, flowers and seed pods, all culture media including any and all compositions, comprising all auxins and all cytokinins of any concentration, all Agrobacterium including Agrobacterium tumefaciens and Agrobacterium rhizogenes, all vectors, all antibiotics, all selective markers, all scorable markers, and all plant parts, including callus, tissue, seeds, or progeny .

*The state of the art and the unpredictability thereof*: Applicant acknowledges that transformation and regeneration techniques developed for most dicot and monocot plants have been unsuccessful for members of the family Linaceae, particularly flax (specification, p. 3 lines 5-7).

Plant transformation is unpredictable. According to Hansen, "[P]lant transformation is an art because of the unique culture conditions required for each crop species. To accommodate a genotype or species that has not been manipulated in culture previously, one must either adapt an established protocol or create a new one", (Hansen et. al., 1999, Trends in plant Science, vol 4, pages 226-231, see page 230). Applicant has given no guidance or working examples of DNA introduction by particle bombardment or by microinjection.

Agrobacterium-mediated transformation of monocots is particularly unpredictable. Early attempts largely failed, due to failure to identify transformation-competent and regenerable cells (see, e.g., Potrykus, Gene Transfer to Cereals: An Assessment, 1990, Biotechnology, 8(6): 535-542 p. 538, column 2, 3rd full ¶ ). When success is observed, the transformation appear to be

transient only (see, e.g., Narasimhulu et. al., 1996, The Plant Cell, Early transcription of Agrobacterium T-DNA genes in tobacco and maize, vol. 8, p. 874, column 2, top ¶; p. 873, column 2, first full ¶).

A number of variable are known in the art which influence Agrobacterium mediated transformation and the regeneration of the tissue to whole plants: The specific stain of Agrobacterium used, the concentration of Agrobacterium used in cocultivation, the time and conditions of cocultivation, the plant tissue used in the cocultivation, the medium used and treatment conditions, including time duration, compositions, and concentration of reagents, for each step of the method. While the specification can provide clarification of elements which are known to one skilled in the art, *essential steps and conditions not known to one of ordinary skill in the art are unpredictable,* and must be recited in the claims. To define the specific stain of Agrobacterium used, the concentration of Agrobacterium used in cocultivation, the time and conditions of cocultivation, the plant tissue and explant used in the cocultivation, the medium used and treatment conditions, including time duration, compositions, and concentration of reagents, for each and all the steps of the method would requires a myriad of different combinations, subcombinations, and permutations of the variables. Applicant has provided no guidance on how to predictably eliminate inoperable embodiments from a virtually ad infinitum of possibilities other than by random trial and error, which is excessive experimentation and an undue burden.

*Working Examples*: Applicant teaches Agrobacterium mediated transformation of flax hypocotyls by coculturing Agrobacterium bearing a binary

vector containing a neomycin phosphotransferase gene, cocultivation of Agrobacterium and hypocotyl segments for 4 days, transfer of cocultured material to media containing a combination of auxins and cytokinins and kanamycin, transferring selected calli or shoot to medium containing a second antibiotic, G-418, and rooting selected calli or shoots to produce a whole plant, as described in the specification (pages 20, Example 2, through page 28).

*Experimentation required:* Multitudes of experiments would be required to determine which Agrobacterium to use as transfer agent, under what conditions to perform the cocultivation including treatment duration time, temperature, which coculture medium, and whether it contains vir inducers such as acetosyringone to produce the desired result. Additionally, many experiments would be required to determine which plant cells, such as suspension cells or explant tissue cells, and if explant cells, what explant, including callus, root, shoot, stem, leaf, seed , embryos or flowers, would work as desired with Agrobacterium mediated transformation conditions of above. A plethora of experiments incorporating all the permutations and combinations of the above would be required to determine which plant selection medium, containing what hormones, if any, which auxins and cytokinins, at what concentrations and in which order, and which antibiotic(s) at what concentration and in which order, would function as desired. Applicant must provide sufficient guidance to address these issues. Without such guidance the experimentation required would not be routine, but would be undue. This would impose a burden on the skilled artesian, without a reasonable expectation of success.

In view of the breadth of the claims (all Linum genus plants, including linseed, flax, and Linus usitatissimum, all explants including leaves, roots, stems, hypocotyls, flowers and seed pods, all culture media including any and all compositions comprising all auxins and all cytokinins of any concentration, all Agrobacterium including Agrobacterium tumefaciens and Agrobacterium rhizogenes, all vectors, all antibiotics in any combination or sequential order, all selective markers, all scorable markers, and all plant parts, including callus, tissue, seeds, or progeny), the nature of the invention, the unpredictability of the art, the lack of guidance in the specification, undue trial and error experimentations would be required to enable the invention as commensurate in scope with the claims.

***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-5, 7-9, 11, 13-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Bretagne-Sagnard, et. al., (Selection of transgenic flax plants is facilitated by spectinomycin, Transgenic Research, Vol. 5, pages 131-137, 1996).

Bretagne-Sagnard, et. al. teach a method for generating transgenic plants of the genus Linum comprising introducing a recombinant DNA binary vector (p. 132, 6th full ¶) comprising a selectable marker which confers resistance to at least one antibiotic (kanamycin) into hypocotyl cells of a flax plant, induction a transgenic callus from the cells thereof (p. 135, lines 1-5), and regenerating transgenic flax plants (p. 135, 2nd and 3rd full ¶s) after culturing the calli on a medium containing kanamycin, and transferring the calli or shoots onto a medium containing cefotaxime (p. 132, 5th full ¶), a second antibiotic which is different from the kanamycin, the first antibiotic, the first antibiotic at 200 mg/l (p. 132, final ¶), and the second antibiotic at 100 mg/l (p. 132, 5th full ¶). Bretagne-Sagnard, et. al. also teach a selectable marker gene coding neomycin phosphotransferase (p. 132, 5th full ¶) operably linked to expression control regions (p. 132, 5th ¶) introduction of the DNA by Agrobacterium tumefaciens, a medium containing the first antibiotic containing the auxin, NAA, at (>0.05,g/l) and the cytokinin TDZ or BAP at (>0.002 mg/l), a medium containing the second antibiotic and free of auxins or cytokinins (p. 133, lines 2-4; rooting medium is routinely free of plant hormones), a DNA encoding a GUS gene as an additional scorable marker (p. 132 5th full ¶ ), and transgenic plant cells, callus, tissues or plants (p. 135, Table 1).

Accordingly Bretagne-Sagnard, et. al. anticipate the claimed invention.

***Claim Rejections - 35 USC § 103***

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 1-9 and 11-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bretagne-Sagnard, et. al., Selection of transgenic flax plants is facilitated by spectinomycin, Transgenic Research, Vol. 5, pages 131-137 (1996) as discussed above for claims 1-5, 7-9, 11, 13-25, in view of Stachel, et. al., Identification of the signal molecules produced by wounded plant cells that activate T-DNA transfer in Agrobacterium tumefaciens, Nature vol. 318: 624-629, 1985.

Bretagne-Sagnard, et. al., do not teach the use of kanamycin as the first antibiotic and G-418 as the second antibiotic.

Bretagne-Sagnard, et. al., do teach the use of the antibiotic G-418 as a selective agent (p. 132, 6$^{th}$ and 8$^{th}$ ¶s). It is notorious well known that kanamycin and G418 are alternative selective antibiotic agents . It would have been obvious to one of skill in the art, at the time of the invention was made, to substitute for the cefotaxime of Bretagne-Sagnard, et. al., the use of G418 as a different antibiotic. One skilled in the art would have been motivated to so, with a reasonable expectation of success. Accordingly, the claimed invention is prima facie obvious in view of the prior art.

Bretagne-Sagnard, et. al., does not teach the presence of acetosyringone with the Agrobacterium. Stachel teaches the use of acetosyringone (Stachel, et. al., Identification of the signal molecules produced by wounded plant cells that

activate T-DNA transfer in Agrobacterium tumefaciens, Nature vol. 318: 624-629, 1985). Acetosyringone is compound well known to activate T-DNA transfer from Agrobacterium It would have been obvious to one of skill in the art, at the time of the invention was made, to combine the acetosyringone of Stachel with the Agrobacterium of Bretagne-Sagnard, et. al., to enhance the Agrobacterium transformation. Accordingly, the claimed invention is prima facie obvious in view of the prior art

The choice of using synchronized germinating seeds is mere optimization of process parameters and an obvious design choice. Accordingly the claimed invention is prima facie obvious in view of the prior art.

***Remarks***

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Georgia L. Helmer whose telephone number is 571-272-0976. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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May 18, 2004

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